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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Effect of a significant asymptomatic unilateral carotid artery stenosis on outcomes in patients undergoing coronary artery bypass grafting

Ewa Podolecka[1], Wojciech Wańha[1], Aleksandra Michalewska-Włudarczyk[1], Witold Włudarczyk[1], Ryszard Bachowski[2], Marek Deja[2], Maciej Kaźmierski[1]

[1]Third Department of Cardiology, Upper Silesian Centre of Cardiology, Medical University of Silesia, Katowice, Poland
[2]Department of Cardiac Surgery, Upper Silesian Centre of Cardiology, Medical University of Silesia, Katowice, Poland

Abstract

Background: Occurrence of a stroke is a major concern in patients undergoing coronary artery bypass grafting (CABG). It remains uncertain whether significant asymptomatic carotid artery stenosis (CAS) is associated with stroke incidence in such patients.

Aim: To investigate the incidence of cerebrovascular events, myocardial infarction (MI), and death in patients with a significant asymptomatic CAS undergoing CABG.

Methods: We prospectively evaluated 123 consecutive patients with documented carotid artery duplex Doppler ultrasound examination who underwent isolated CABG. Patients with a significant (≥ 60%) asymptomatic unilateral CAS (n = 35) were compared with those without a significant CAS (n = 88) to assess the rates of stroke, MI and mortality after CABG.

Results: No significant differences between patients with a significant asymptomatic unilateral CAS and those without a significant CAS in regard to age (p = 0.5955), presence of hypertension (p = 0.2343), diabetes (p = 0.5495), smoking (p = 0.7891), serum creatinine (p = 0.47) and left ventricular systolic function as evaluated by ejection fraction (p = 0.3789). No cerebrovascular events, MI and deaths occurred during the first 30 days postoperatively. At 12 months, no differences were seen between the groups in the incidence of MI (p = 0.1005) and mortality (p = 0.3959). However, a trend towards higher stroke incidence was noted among patients with a significant asymptomatic unilateral CAS (p = 0.0692). The primary combined endpoint (stroke, MI, and mortality) occurred in 40% of patients with a significant asymptomatic unilateral CAS and 17.05% of patients without a significant CAS (p = 0.0097). Linear regression analysis showed an association between significant asymptomatic unilateral CAS and stroke (p = 0.0041), and between significant asymptomatic unilateral CAS and the primary end point (p = 0.0475).

Conclusions: The presence of a significant asymptomatic unilateral CAS does not increase the risk of stroke, MI and mortality within 30 days after CABG but is was associated with an increased risk of cardiovascular events during the first 12 months postoperatively.

Key words: carotid artery stenosis, coronary artery disease, coronary artery bypass grafting

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INTRODUCTION

Atherosclerosis is a multifactorial systemic disease process that mostly affects coronary arteries but may also develop in other vascular beds, particularly in carotid and lower limb arteries. Carotid artery atherosclerosis often accompanies significant coronary atherosclerotic lesions [1–3]. In patients undergoing coronary artery bypass grafting (CABG), concomitant carotid artery atherosclerosis is associated with an increased risk of neurological complications, particularly ischaemic stroke [4, 5]. The prevalence of > 50% carotid artery stenosis (CAS) among patients undergoing CABG has been estimated at 4–15% [6]. According to the European Society

Address for correspondence:
Ewa Podolecka, MD, PhD, Third Department of Cardiology, Upper Silesian Centre of Cardiology, Medical University of Silesia, ul. Ziołowa 45/47, 40–635 Katowice, Poland, e-mail: epodolecka@interia.pl

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of Cardiology guidelines, CAS is considered symptomatic if a transient ischaemic attack (TIA) or stroke developed in the supplied area within the last 6 months [7]. Revascularisation is recommended in patients with symptomatic ≥ 70% CAS (TIA/stroke within 6 months, a class Ic recommendation) and may be considered in patients with asymptomatic bilateral ≥ 70% CAS (a class IIb recommendation) [7].

In contrast, no clear recommendations were offered for patients with a significant asymptomatic unilateral CAS before planned CABG.

Stroke is a major life-threatening complication of CABG. The incidence of stroke after CABG is 1.3–4.3% [8, 9]. It has been estimated that the risk of stroke in patients with asymptomatic > 50% CAS is 2–3% [10]. This risk increases with the severity of atherosclerotic lesions and is significantly higher among those with > 80–89% stenosis. Norris et al. [11, 12] showed that among patients with asymptomatic ≤ 75% CAS, the risk of stroke is small (1.3%/years) but it increases significantly to 3.3%/year in those with 75–90% stenosis.

The aim of our study was to evaluate prospectively whether the presence of a concomitant significant asymptomatic unilateral internal CAS affected the risk of individual endpoints of stroke, myocardial infarction (MI), and death, and the risk of a combined endpoint (stroke, MI, and death) at 1-month and 1-year follow-up after CABG.

METHODS

Study design

The study was performed in the Third Department of Cardiology at the Upper Silesian Centre of Cardiology in Katowice in 2008–2009. We evaluated 155 consecutive patients referred for elective isolated CABG due to multivessel coronary artery disease from February to July 2008. We excluded patients with significant valvular heart disease, significant symptomatic CAS, and a history of carotid artery revascularisation. The final study group included 123 patients. The study population was divided into two groups depending on the presence or absence of a ≥ 60% internal CAS. Group I included patients with a asymptomatic unilateral ≥ 60% internal CAS, and Group II included patients with asymptomatic < 60% internal CAS. None of the studied subjects underwent carotid artery revascularisation during 1-year follow-up. At 1 month and 1 year after CABG, all patients (or their caregivers, if applicable) were contacted by phone and information was sought regarding complications including stroke, MI, and death.

Carotid artery ultrasonography

Duplex Doppler carotid artery ultrasonography was performed in all patients before CABG to screen for vascular lesions. Ultrasonography was performed using a Sonos 7500 system (Hewlett Packard) with a 10 MHz vascular probe. The common, internal, and external carotid artery was evaluated in real-time in 2 planes (sagittal and transverse) using both duplex and colour Doppler. During pulse wave Doppler examination, the interrogation angle was set below 60°. Sagittal and transverse B-mode images were recorded, along with colour and duplex Doppler images in the sagittal plane. Standard measurement locations included the common carotid artery 2 cm before the bifurcation, external carotid artery, and proximal and distal internal carotid artery. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) of blood flow were measured in the selected locations [13]. Based on the North American Symptomatic Carotid Endarterectomy Trial (NASCET) criteria which are currently most commonly cited in the literature, a significant stenosis (> 60%) was defined as PSV > 230 cm/s, EDV ≥ 100 cm/s and the internal carotid artery to common carotid artery peak velocity ratio of > 2.0 [13].

Coronary artery bypass grafting

CABG was performed using cardiopulmonary bypass with pulsatile flow as the standard approach and the target mean systemic arterial pressure of 70–80 mm Hg. Blood products were not transfused during the preoperative and perioperative period, and 3 patients required transfusion during the postoperative period, including 2 patients without significant CAS and 1 patient with a significant asymptomatic unilateral internal CAS. None of the studied subjects was reoperated.

Statistical analysis

Statistical analysis was performed using the GraphPad InStat software, version 3.05. Data were shown as mean values and standard deviations. Quantitative variables were compared using the Student t test. Distribution of qualitative variables was compared using the Fisher and χ^2 tests. A linear regression model was used to examine the association between a significant asymptomatic unilateral internal CAS and stroke, and between a significant internal CAS and a combined endpoint of stroke, MI, and death. A multivariate linear regression model was used to identify predictors of stroke. $P < 0.05$ was consider statistically significant.

RESULTS

Group I included 35 patients with a significant asymptomatic unilateral 60–99% stenosis of the internal carotid artery, and group II included 88 patients with nonsignificant (< 60%) atherosclerotic lesions in the internal carotid artery. Demographic and clinical characteristics of the study group are shown in Table 1. In group I, the mean lumen stenosis was 69.2% in the right internal carotid artery and 69.9% in the left internal carotid artery. No neurological (TIA/stroke) or cardiovascular complications were noted in both groups at one month after CABG. At 1 year, a trend towards a higher incidence of stroke ($p = 0.692$) was noted in patients with ≥ 60% stenosis of the internal carotid artery (Table 2). No significant differences were seen between the groups in the incidence of MI ($p = 0.1005$) and mortality ($p = 0.3959$) (Table 2). The combined endpoint

Table 1. Demographic and clinical characteristics of the study group

Variable	Group I (n = 35)	Group II (n = 88)	P
Men/women	25/10	66/22	0.8201
Age [years]	65.31 ± 8.44	64.33 ± 9.55	0.5955
Hypertension	85.7%	75%	0.2343
Type 2 diabetes	51.4%	44.3%	0.5495
Total cholesterol [mg/dL]	168.91 ± 37.21	177.89 ± 37.56	0.2343
HDL cholesterol [mg/dL]	44.97 ± 13.41	44.89 ± 12.83	0.9768
Triglycerides [mg/dL]	133.11 ± 51.75	149.95 ± 125.55	0.4454
LDL cholesterol [mg/dL]	99.46 ± 29.30	103.23 ± 31.19	0.5423
Creatinine [mg/dL]	1.06 ± 0.28	1.03 ± 0.23	0.4700
Smokers	22.8%	29.6%	0.7891
Peripheral arterial disease	8.6%	11.4%	0.7564
Previous myocardial infarction	37.1%	42%	0.6868
Left ventricular ejection fraction [%]	50.65 ± 10.23	48.87 ± 9.81	0.3789
Three-vessel disease	62.9%	63.6%	0.8565

Table 2. Complications after coronary artery bypass grafting

Endpoint	Group I (n = 35)	Group II (n = 88)	P
Stroke	8.6%	1.1%	0.0692
Myocardial infarction	11.4%	3.4%	0.1005
Death	20%	12.5%	0.3959
Combined endpoint (stroke, myocardial infarction, death)	40%	17.05%	0.0097

of stroke, MI, and death was more common among those with a significant asymptomatic unilateral internal CAS compared to the control group (40% vs. 17.05%, p = 0.0097) (Table 2). Linear regression analysis showed an association between a significant internal CAS and stroke (p = 0.0041), and between a significant internal CAS and the combined endpoint of stroke, MI, and death (p = 0.0475). Multivariate linear regression analysis confirmed the association between a significant asymptomatic unilateral internal CAS and stroke (p = 0.0467) (Table 3).

DISCUSSION

The risk of stroke among patients undergoing CABG is affected by multiple factors including age, concomitant heart failure, valvular heart disease, involvement of the left main coronary artery, duration of surgical procedure, postoperative atrial fibrillation, reoperation, and a history of MI, stroke, or TIA [4, 10, 14–16].

Advanced age is a major risk factor for stroke in the general population [15, 16]. Schachner et al. [17] showed an association between age and the risk of stroke after CABG. It has been estimated that in patients above 75 years of age with established carotid artery disease who are referred for CABG, the risk of stroke is about 9% [10]. Chronic kidney disease is another risk factor for stroke after CABG, as shown

Table 3. Independent predictors of stroke in a multivariate linear regression model

Dependent variable	Independent variables	Standardized regression coefficient	P
Stroke Adjusted R^2 = 0.06 Adjusted p = 0.0467	Significant asymptomatic unilateral internal carotid artery stenosis	2.8130	0.0059
	Age	0.3261	0.7450
	Serum creatinine level	0.4471	0.6557
	Type 2 diabetes	1.7180	0.0887
	Hypertension	0.9665	0.3360
	Left ventricular ejection fraction	0.0391	0.9689
	Peripheral arterial disease	1.5420	0.1260

by Stamou et al. [4] and Naylor et al. [5]. In a large study of more than 16,500 post-CABG patients, renal failure was an indepedent risk factor for stroke [5]. Peripheral arterial disease is also a risk factor for stroke, as confirmed by Antunes et al. [15] and other authors in patients after isolated CABG [16–18]. An increased risk of stroke is also associated with left ventricular systolic dysfunction [4, 15, 16]. In addition, a history of MI or stroke is a risk factor for recurrent neurological incident [4, 15, 16]. Stamou et al. [4] showed that the risk of stroke was increased threefold in patients who suffered a MI within 24 h before CABG. It appears that an increased prothrombotic activity, sympathetic activation, and haemodynamic instability contribute to an increased risk of stroke in patients after a MI [4]. In addition, the extent of the surgical procedure affects the occurrence of neurological complications. Numerous studies have shown that in patients undergoing valvular surgery or combined coronary artery and valvular surgery, the risk of stroke is increased compared to patients undergoing isolated CABG [19]. In a prospective study of more than 16,000 patients, the risk of stroke was lowest in the isolated CABG group (3.8% compared to 7.4% among patients undergoing combined valvular and CABG surgery) [19]. The risk of stroke in patients undergoing CABG is also affected by the volume of transfused blood products. Mikkola et al. [20] showed that transfusion of blood products increase the risk of stroke in patients after CABG.

A stenosis of the internal carotid artery is an adverse prognostic factor. Revascularisation is recommended for significant symptomatic internal CAS [7]. In the NASCET study and the Medical Research Council European Carotid Surgery Trial, benefits of endarterectomy were shown in patients with a symptomatic significant (≥ 70%) CAS before the planned surgery [21, 22]. However, the optimal management approach is not clear in patients with a significant asymptomatic unilateral CAS, particularly before planned CABG [23].

In the present study, we attempted to examine the effect of a significant asymptomatic unilateral internal CAS on patient outcomes at 1 month and 1 year after CABG. Based on the NASCET study criteria, a significant internal carotid artery stenosis was defined as ≥ 60% [24]. The evaluated group of patients with a significant asymptomatic unilateral internal CAS did not differ from the control group in regard to established risk factors for stroke such as age, serum creatinine level, concomitant peripheral arterial disease, left ventricular systolic function, and a history of MI before CABG (Table 1). In addition, none of the subjects in both groups had suffered a previous stroke or TIA.

At 1-month follow-up after CABG, we found no neurological complications, MI, and death in both patients with a significant asymptomatic unilateral internal CAS and patients in the control group. Similar results were reported by Ghosh et al. [25] who found no increase in the 30-day postoperative stroke risk in patients after isolated CABG compared to the control group. Available data indicate that a significant asymptomatic unilateral CAS is associated with a low risk of stroke early after CABG. During a 30-day follow-up of 61 patients with a unilateral, asymptomatic 70–99% stenosis of the internal carotid artery who were referred for isolated CABG, valve replacement, or combined valvular and CABG surgery, Baiou et al. [26] reported not a single case of stroke. In a retrospective single-centre study in patients referred for isolated CABG, Manabe et al. [27] also showed no effect of a significant asymptomatic CAS on the incidence of stroke as compared to the control group. Among 461 patients with a asymptomatic unilateral CAS, 67% of patients had a moderate stenosis (50–70%), 15% of patients had a severe stenosis (80–99%), and the internal carotid artery was occluded in 18% of patients [27]. Similar results were reported by Mahmoudi et al. [28] who showed that a significant asymptomatic CAS did not increase the 30-day risk of stroke and all-cause mortality among patients undergoing isolated CABG. In that group of more than 800 patients with a significant asymptomatic CAS, the mean age was higher, and peripheral arterial disease and heart failure were more prevalent compared to patients without significant carotid artery lesions but the risk of stroke was similar [28].

In contrast, the presence of an asymptomatic internal CAS was associated with an increased risk of stroke, MI, and death at 1 year of follow-up. The incidence of the combined endpoint of stroke, MI, and death was higher among patients with a significant asymptomatic internal CAS compared to the control group (Table 2).

Linear regression analysis showed an association between a significant asymptomatic unilateral internal CAS and stroke, and between a significant internal CAS and the combined endpoint of stroke, MI, and death. In addition, multivariate linear regression analysis confirmed the association between a significant asymptomatic unilateral internal CAS and stroke ($p = 0.0467$) (Table 3).

Our findings may suggest that patients with a significant asymptomatic unilateral internal CAS require carotid artery revascularisation. The ongoing CABACS study is a randomised, multicentre trial evaluating patients with a significant asymptomatic CAS referred for CABG [29]. It is hoped that the results of that study will help clarify the optimal management approach to patients with asymptomatic carotid artery disease before planned CABG.

CONCLUSIONS

A significant asymptomatic unilateral internal CAS is associated with an increased risk of stroke, MI, and death in patients after CABG at 1-year follow-up.

Conflict of interest: *none declared*

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Wpływ istotnego jednostronnego bezobjawowego zwężenia tętnic szyjnych na rokowanie pacjentów leczonych operacyjnie z powodu choroby wieńcowej

Ewa Podolecka[1], Wojciech Wańha[1], Aleksandra Michalewska-Włudarczyk[1], Witold Włudarczyk[1], Ryszard Bachowski[2], Marek Deja[2], Maciej Kaźmierski[1]

[1]III Oddział Kardiologii, Górnośląski Ośrodek Kardiologii, Śląski Uniwersytet Medyczny, Katowice
[2]Oddział Kardiochirurgii, Górnośląski Ośrodek Kardiologii, Śląski Uniwersytet Medyczny, Katowice

Streszczenie

Wstęp: Zwężenie tętnic szyjnych (CAS) często współistnieje ze zmianami miażdżycowymi tętnic wieńcowych. Objawowe CAS zwiększa ryzyko powikłań neurologicznych u chorych poddawanym pomostowaniu aortalno-wieńcowemu (CABG). W przypadku bezobjawowego CAS zarówno ryzyko, jak i sposób postępowania z chorym przed planowanym CABG nie zostały jednoznacznie określone.

Cel: Celem pracy była prospektywna ocena wpływu istotnego jednostronnego bezobjawowego zwężenia tętnicy szyjnej wewnętrznej na występowanie pojedynczego punktu końcowego (obejmującego udar mózgu, zawał serca [MI] i zgon) oraz złożonego punktu końcowego (obejmującego udar mózgu, MI i zgon) w obserwacji miesięcznej i rocznej po CABG.

Metody: Analizie poddano 155 kolejnych pacjentów zakwalifikowanych w okresie od lutego do lipca 2008 r. w trybie planowym do selektywnej operacji CABG z powodu stabilnej wielonaczyniowej choroby wieńcowej. Z badania wykluczono chorych z istotnymi wadami zastawkowymi oraz istotnymi objawowymi CAS, a także tych, u których wcześniej przeprowadzono zabieg rewaskularyzacji tętnic szyjnych. U wszystkich pacjentów wykonano przed CABG ultrasonografię doplerowską tętnic szyjnych. Badaną populację podzielono na dwie grupy. Kryterium podziału stanowiło zwężenie tętnicy szyjnej wewnętrznej ≥ 60%. Grupa I obejmowała pacjentów z jednostronnym bezobjawowym ≥ 60% zwężeniem tętnicy szyjnej wewnętrznej, a grupa II — chorych z bezobjawowym zwężeniem tętnicy szyjnej wewnętrznej < 60%. Żadna z badanych osób nie była poddana zabiegowi rewaskularyzacji tętnic szyjnych w rocznym okresie pooperacyjnym.

Wyniki: Grupa I liczyła 35 osób z jednostronnym bezobjawowym istotnym (60–99%) zwężeniem w obrębie tętnicy szyjnej wewnętrznej, a grupa II — 88 osoby ze zmianami miażdżycowymi w tętnicy szyjnej wewnętrznej < 60%. Między grupami nie zaobserwowano różnic pod względem: wieku (65,31 ± 8,44 *vs.* 64,33 ± 9,55 roku; p = 0,5955), częstości występowania nadciśnienia tętniczego (p = 0,2343), cukrzycy (p = 0,5495) i palenia tytoniu (p = 0,7891). Badane grupy nie różniły się stężeniem cholesterolu całkowitego (168,91 ± 37,21 *vs.* 177,89 ± 37,56 mg/dl; p = 0,2343), cholesterolu frakcji HDL (44,97 ± 13,41 *vs.* 44,89 ± 12,83 mg/dl; p = 0,9768), triglicerydów (133,11 ± 51,75 *vs.* 149,95 ± 125,55 mg/dl; p = 0,4454), cholesterolu frakcji LDL (99,46 ± 29,30 vs. 103,23 ± 31,19 mg/dl; p = 0,5423) i kreatyniny (1,06 ± 0,28 vs. 1,03 ± 0,23 mg/dl; p = 0,47). Ponadto funkcja skurczowa lewej komory (LVEF) była porównywalna w obu grupach (50,65 ± 10,23% *vs.* 48,87 ± 9,81%; p = 0,3789). W obserwacji miesięcznej nie stwierdzono powikłań sercowo-naczyniowych po CABG. W obserwacji rocznej nie wykazano istotnych różnic między badanymi grupami pod względem częstości występowania MI (p = 0,1005) i zgonu (p = 0,3959). Natomiast w grupie I wykazano trend w kierunku częstszego występowania udaru mózgu (p = 0,0692). Złożony punkt końcowy obejmujący udar mózgu, MI i zgon częściej występował w grupie I w porównaniu z grupą kontrolną (p = 0,0097). W badaniu regresji liniowej wykazano związek między istotnym jednostronnym bezobjawowym zwężeniem tętnicy szyjnej wewnętrznej a udarem mózgu (p = 0,0041), a także między istotnym zwężeniem tętnicy szyjnej wewnętrznej a złożonym punktem końcowym obejmującym udar mózgu, MI i zgon (p = 0,0475). W analizie wieloczynnikowej regresji liniowej potwierdzono zależność między istotnym jednostronnym bezobjawowym zwężeniem tętnicy szyjnej wewnętrznej a udarem mózgu (p = 0,0467).

Wnioski: 1. Istotne jednostronne bezobjawowe zwężenie tętnicy szyjnej wewnętrznej nie zwiększa częstości zdarzeń sercowo-naczyniowych w obserwacji miesięcznej u chorych leczonych za pomocą CABG z powodu stabilnej choroby wieńcowej. 2. Obecność istotnego jednostronnego bezobjawowego zwężenia tętnicy szyjnej wewnętrznej wiąże się z częstszym występowaniem udaru mózgu i złożonego punktu końcowego obejmującego udar mózgu, MI i zgon u chorych po CABG w obserwacji rocznej.

Słowa kluczowe: zwężenie tętnic szyjnych, choroba wieńcowa, pomostowanie aortalno-wieńcowe

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Adres do korespondencji:
dr n. med. Ewa Podolecka, III Oddział Kardiologii, Górnośląski Ośrodek Kardiologii, Śląski Uniwersytet Medyczny, ul. Ziołowa 45/47, 40–635 Katowice, e-mail: epodolecka@interia.pl
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